CLAIMS

1. A method for regulating a conversion rate of a hereditary trait of a cell, comprising the step of:

(a) regulating an error-prone frequency of gene replication of the cell.

2. A method according to claim 1, wherein at least two kinds of error-prone frequency agents playing a role in the gene replication are present.

3. A method according to claim 2, wherein at least about 30% of the error-prone frequency agents have a lesser error-prone frequency.

4. A method according to claim 1, wherein the agents playing a role in the gene replication have heterogeneous error-prone frequencies.

5. A method according to claim 1, wherein the agent having the lesser error-prone frequency is substantially error-free.

6. A method according to claim 2, wherein the error-prone frequencies are different from each other by at least 10^1.

7. A method according to claim 2, wherein the error-prone frequencies are different from each other by at least 10^2.

8. A method according to claim 2, wherein the error-prone frequencies are different from each other by at least 10^3.

9. A method according to claim 1, wherein the step of

regulating the error-prone frequency comprises regulating an error-prone frequency of at least one agent selected from the group consisting of a repair agent capable of removing abnormal bases and a repair agent capable of repairing mismatched base pairs, the agents being present in the cell.

10. A method according to claim 1, wherein the step of regulating the error-prone frequency comprises providing a difference in the number of errors between one strand and the other strand of double-stranded genomic DNA in the cell.

11. A method according to claim 1, wherein the step of regulating the error-prone frequency comprises regulating an error-prone frequency of a DNA polymerase of the cell.

12. A method according to claim 11, wherein the DNA polymerase has a proofreading function.

13. A method according to claim 11, wherein the DNA polymerase comprises at least one polymerase selected from the group consisting of DNA polymerase α, DNA polymerase β, DNA polymerase γ, DNA polymerase δ, and DNA polymerase ε of eukaryotic cells, and corresponding DNA polymerases thereto.

14. A method according to claim 1, wherein the step of regulating the error-prone frequency comprises regulating proofreading activity of at least one polymerase selected from the group consisting of DNA polymerase δ and DNA polymerase ε of eukaryotic cells, and corresponding DNA polymerases thereto.

15. A method according to claim 1, wherein the regulating

the error-prone frequency comprises regulating a proofreading activity of DNA polymerase δ of a prokaryotic cell or DNA polymerase corresponding thereto.

16. A method according to claim 1, wherein the regulating the error-prone frequency comprises introducing a DNA polymerase variant into the cell.

17. A method according to claim 16, wherein the introducing the DNA polymerase variant into the cell is performed with a method selected from the group consisting of homologus recombination and transformation using gene introduction or a plasmid.

18. A method according to claim 1, wherein the regulating the error-prone frequency comprises introducing a variant of DNA polymerase δ of a prokaryotic cell or DNA polymerase corresponding thereto.

19. A method according to claim 18, wherein the variant of DNA polymerase δ of a prokaryotic cell or DNA polymerase corresponding thereto comprises a mutation which deletes a proofreading activity thereof.

20. A method according to claim 1, wherein the step of regulating the error-prone frequency comprises increasing the error-prone frequency higher than that of a wild type of the cell.

21. A method according to claim 12, wherein the proofreading function of the DNA polymerase is lower than that of a wild type of the DNA polymerase.

22. A method according to claim 12, wherein the proofreading function of the DNA polymerase provides at least one mismatched base in a base sequence, the number of the at least one mismatched base being greater by at least one than that of a wild type of the DNA polymerase.

23. A method according to claim 12, wherein the proofreading function of the DNA polymerase provides at least one mismatched base in a base sequence.

24. A method according to claim 12, wherein the proofreading function of the DNA polymerase provides at least two mismatched bases.

25. A method according to claim 12, wherein the proofreading function of the DNA polymerase provides at least one mismatched base in a base sequence at a rate of 10^{-6}.

26. A method according to claim 12, wherein the proofreading function of the DNA polymerase provides at least one mismatched base in a base sequence at a rate of 10^{-3}.

27. A method according to claim 12, wherein the proofreading function of the DNA polymerase provides at least one mismatched base in a base sequence at a rate of 10^{-2}.

28. A method according to claim 1, wherein the cell is a gram-positive or eukaryotic cell.

29. A method according to claim 1, wherein the cell is a eukaryotic cell.

30. A method according to claim 1, wherein the cell is a

unicellular or multicellular organism.

31. A method according to claim 1, wherein the cell is an animal, plant, fungus, or yeast cell.

32. A method according to claim 1, wherein the cell is a mammalian cell.

33. A method according to claim 1, wherein after conversion of the hereditary trait, the cell has substantially the same growth as that of a wild type of the cell.

34. A method according to claim 1, wherein the cell naturally has at least two kinds of polymerases.

35. A method according to claim 1, wherein the cell naturally has at least two kinds of polymerases, the at least two kinds of polymerases having a different error-prone frequency.

36. A method according to claim 1, wherein the cell has at least two kinds of polymerases, one of the at least two kinds of polymerases is involved in an error-prone frequency of a lagging strand, and another of the at least two kinds of polymerases is involved in an error-prone frequency of a leading strand.

37. A method according to claim 1, wherein the cell has resistance to an environment, the resistance being not possessed by the cell before the conversion.

38. A method according to claim 37, wherein the environment comprises, as a parameter, at least one agent selected from the group consisting of temperature, humidity, pH, salt

concentration, nutrients, metal, gas, organic solvent, pressure, atmospheric pressure, viscosity, flow rate, light intensity, light wavelength, electromagnetic waves, radiation, gravity, tension, acoustic waves, cells other than the cell, chemical agents, antibiotics, natural substances, mental stress, and physical stress, or a combination thereof.

39. A method according to claim 1, wherein the cell includes a cancer cell.

40. A method according to claim 1, wherein the cell constitutes a tissue.

41. A method according to claim 1, wherein the cell consititues an organism.

42. A method according to claim 1, further comprising:

differentiating the cell to a tissue or an organism after conversion of the hereditary trait of the cell.

43. A method according to claim 1, wherein the error-prone frequency is regulated under a predetermined condition.

44. A method according to claim 43, wherein the error-prone frequency is regulated by regulating at least one agent selected from the group consisting of temperature, humidity, pH, salt concentration, nutrients, metal, gas, organic solvent, pressure, atmospheric pressure, viscosity, flow rate, light intensity, light wavelength, electromagnetic waves, radiation, gravity, tension, acoustic waves, cells other than the cell, chemical agents, antibiotics, natural substances, mental stress, and physical stress, or a

combination thereof.

45. A method for producing a cell having a regulated hereditary trait, comprising the step of:

(a) regulating an error-prone frequency of gene replication of the cell; and

(b) reproducing the resultant cell.

46. A method according to claim 45, further comprising:

screening for the reproduced cell having a desired trait.

47. A method according to claim 45, wherein at least two kinds of error-prone frequency agents playing a role in the gene replication are present.

48. A method according to claim 45, wherein at least about 30% of the error-prone frequency agents have a lesser error-prone frequency.

49. A method according to claim 45, wherein the agents playing a role in the gene replication have heterogeneous error-prone frequencies.

50. A method according to claim 45, wherein the agent having the lesser error-prone frequency is substantially error-free.

51. A method according to claim 45, wherein the error-prone frequencies are different from each other by at least 10^1.

52. A method according to claim 45, wherein the error-prone frequencies are different from each other by at least 10^2.

53. A method according to claim 45, wherein the error-prone frequencies are different from each other by at least 10^3.

54. A method according to claim 45, wherein the step of regulating the error-prone frequency comprises regulating an error-prone frequency of at least one agent selected from the group consisting of a repair agent capable of removing abnormal bases and a repair agent capable of repairing mismatched base pairs, the agents being present in the cell.

55. A method according to claim 45, wherein the step of regulating the error-prone frequency comprises providing a difference in the number of errors between one strand and the other strand of double-stranded genomic DNA in the cell.

56. A method according to claim 45, wherein the step of regulating the error-prone frequency comprises regulating an error-prone frequency of a DNA polymerase of the cell.

57. A method according to claim 56, wherein the DNA polymerase has a proofreading function.

58. A method according to claim 56, wherein the DNA polymerase comprises at least one polymerase selected from the group consisting of DNA polymerase α, DNA polymerase β, DNA polymerase γ, DNA polymerase δ, and DNA polymerase ε of eukaryotic cells, and corresponding DNA polymerases thereto.

59. A method according to claim 45, wherein the step of regulating the error-prone frequency comprises regulating proofreading activity of at least one polymerase selected

from the group consisting of DNA polymerase δ and DNA polymerase ε of eukaryotic cells, and corresponding DNA polymerases thereto.

60. A method according to claim 45, wherein the regulating the error-prone frequency comprises regulating a proofreading activity of DNA polymerase δ of a prokaryotic cell or DNA polymerase corresponding thereto.

61. A method according to claim 45, wherein the regulating the error-prone frequency comprises introducing a DNA polymerase variant into the cell.

62. A method according to claim 61, wherein the introducing the DNA polymerase variant into the cell is performed with a method selected from the group consisting of homologus recombination and transformation using gene introduction or a plasmid.

63. A method according to claim 45, wherein the regulating the error-prone frequency comprises introducing a variant of DNA polymerase δ of a prokaryotic cell or DNA polymerase corresponding thereto.

64. A method according to claim 63, wherein the variant of DNA polymerase δ of a prokaryotic cell or DNA polymerase corresponding thereto comprises a mutation which deletes only a proofreading activity thereof.

65. A method according to claim 45, wherein the step of regulating the error-prone frequency comprises increasing the error-prone frequency higher than that of a wild type of the cell.

66. A method according to claim 57, wherein the proofreading function of the DNA polymerase is lower than that of a wild type of the DNA polymerase.

67. A method according to claim 57, wherein the proofreading function of the DNA polymerase provides at least one mismatched base in a base sequence, the number of the at least one mismatched base being greater by at least one than that of a wild type of the DNA polymerase.

68. A method according to claim 57, wherein the proofreading function of the DNA polymerase provides at least one mismatched base in a base sequence.

69. A method according to claim 57, wherein the proofreading function of the DNA polymerase provides at least two mismatched bases.

70. A method according to claim 57, wherein the proofreading function of the DNA polymerase provides at least one mismatched base in a base sequence at a rate of 10^{-6}.

71. A method according to claim 57, wherein the proofreading function of the DNA polymerase provides at least one mismatched base in a base sequence at a rate of 10^{-3}.

72. A method according to claim 57, wherein the proofreading function of the DNA polymerase provides at least one mismatched base in a base sequence at a rate of 10^{-2}.

73. A method according to claim 45, wherein the cell is a gram-positive or eukaryotic cell.

74. A method according to claim 45, wherein the cell is a eukaryotic cell.

75. A method according to claim 45, wherein the cell is a unicellular or multicellular organism.

76. A method according to claim 45, wherein the cell is an animal, plant, fungus, or yeast cell.

77. A method according to claim 45, wherein the cell is a mammalian cell.

78. A method according to claim 45, wherein after conversion of the hereditary trait, the cell has substantially the same growth as that of a wild type of the cell.

79. A method according to claim 45, wherein the cell naturally has at least two kinds of polymerases.

80. A method according to claim 45, wherein the cell naturally has at least two kinds of polymerases, the at least two kinds of polymerases having a different error-prone frequency.

81. A method according to claim 45, wherein the cell has at least two kinds of polymerases, one of the at least two kinds of polymerases is involved in an error-prone frequency of a lagging strand, and another of the at least two kinds of polymerases is involved in an error-prone frequency of a leading strand.

82. A method according to claim 45, wherein the cell has

resistance to an environment, the resistance being not possessed by the cell before the conversion.

83. A method according to claim 82, wherein the environment comprises, as a parameter, at least one agent selected from the group consisting of temperature, humidity, pH, salt concentration, nutrients, metal, gas, organic solvent, pressure, atmospheric pressure, viscosity, flow rate, light intensity, light wavelength, electromagnetic waves, radiation, gravity, tension, acoustic waves, cells other than the cell, chemical agents, antibiotics, natural substances, mental stress, and physical stress, or a combination thereof.

84. A method according to claim 45, wherein the cell includes a cancer cell.

85. A method according to claim 45, wherein the cell constitutes a tissue.

86. A method according to claim 45, wherein the cell consititues an organism.

87. A method according to claim 45, further comprising:

differentiating the cell to a tissue or an organism after conversion of the hereditary trait of the cell.

88. A method according to claim 45, wherein the error-prone frequency is regulated under a predetermined condition.

89. A method according to claim 88, wherein the error-prone frequency is regulated by regulating at least one agent selected from the group consisting of temperature, humidity,

pH, salt concentration, nutrients, metal, gas, organic solvent, pressure, atmospheric pressure, viscosity, flow rate, light intensity, light wavelength, electromagnetic waves, radiation, gravity, tension, acoustic waves, cells other than the cell, chemical agents, antibiotics, natural substances, mental stress, and physical stress, or a combination thereof.

90. A method for producing an organism having a regulated hereditary trait, comprising the steps of:

(a) regulating the error-prone frequency of gene replication of the organism; and

(b) reproducing the resultant organism.

91. A cell having a regulated hereditary trait, produced by a method according to claim 90.

92. A cell according to claim 91, wherein the cell has substantially the same growth as that of a wild type of the cell.

93. An organism having a regulated hereditary trait, produced by a method according to claim 90.

94. An organism according to claim 93, wherein the organism has substantially the same growth as that of a wild type of the organism.

95. A method for producing a nucleic acid molecule encoding a gene having a regulated hereditary trait, comprising the steps of:

(a) changing an error-prone frequency of gene replication of an organism;

(b) reproducing the resultant organism;

(c) identifying a mutation in the organism; and

(d) producing a nucleic acid molecule encoding a gene having the identified mutation.

96. A nucleic acid molecule, produced by a method according to claim 95.

97. A method for producing a polypeptide encoded by a gene having a regulated hereditary trait, comprising the steps of:

(a) changing an error-prone frequency of gene replication of an organism;

(b) reproducing the resultant organism;

(c) identifying a mutation in the organism; and

(d) producing a polypeptide encoded by a gene having the identified mutation.

98. A polypeptide, produced by a method according to claim 97.

99. A method for producing a metabolite of an organism having a regulated hereditary trait, comprising the steps of:

(a) changing an error-prone frequency of gene replication of an organism;

(b) reproducing the resultant organism;

(c) identifying a mutation in the organism; and

(d) producing a metabolite having the identified mutation.

100. A metabolite, produced by a method according to claim 99.

101. A nucleic acid molecule for regulating a hereditary trait of an organism, comprising:

a nucleic acid sequence encoding a DNA polymerase having a regulated error-prone frequency.

102. A nucleic acid molecule according to claim 101, wherein the DNA polymerase is DNA polymerase δ or ε of eukaryotic organisms, or DNA polymerase corresponding thereto of gram-positive bacteria.

103. A nucleic acid molecule according to claim 101, wherein the DNA polymerase is a variant of DNA polymerase δ or ε of eukaryotic organisms, or DNA polymerase corresponding thereto of gram-positive bacteria, the variant comprising a mutation which deletes only a proofreading activity thereof.

104. A nucleic acid molecule according to claim 101, wherein the DNA polymerase is a variant of DNA polymerase δ of eukaryotic organisms, or DNA polymerase corresponding thereto of gram-positive bacteria, the variant comprising a mutation which deletes only a proofreading activity thereof.

105. A vector, comprising a nucleic acid molecule according to claim 101.

106. A cell, comprising a nucleic acid molecule according to claim 101.

107. A cell according to claim 106, wherein the cell is a eukaryotic cell.

108. A cell according to claim 107, wherein the eukaryotic cell is selected from the group consisting of plants, animals, and yeasts.

109. A cell according to claim 106, wherein the cell is a gram-positive bacterial cell.

110. A cell according to claim 106, wherein the cell is used for regulating a conversion rate of a hereditary trait.

111. An organism, comprising a nucleic acid molecule according to claim 101.

112. A product substance, produced by a cell according to claim 106 or a part thereof.

113. A nucleic acid molecule, contained in a cell according to claim 106 or a part thereof.

114. A nucleic acid molecule according to claim 113, encoding a gene involved in the regulated hereditary trait.

115. A method for testing a drug, comprising the steps of:

testing an effect of the drug using a cell according to claim 106 as a model of disease;

testing an effect to the drug using a wild type of the cell as a control; and

comparing the model of disease and the control.

116. A method for testing a drug, comprising the steps of:

testing an effect of the drug using an organism according to claim 111 as a model of disease;

testing an effect to the drug using a wild type of

the organsm as a control; and

comparing the model of disease and the control.

117. A set of at least two kinds of polymerases for use in regulating a conversion rate of a hereditary trait of an organism, wherein the polymerases have a different error-prone frequency.

118. A set according to claim 117, wherein one of the at least two kinds of polymerases is involved in an error-prone frequency of a lagging strand, and another of the at least two kinds of polymerases is involved in an error-prone frequency of a leading strand.

119. A set according to claim 117, wherein the set of polymerases are derived from the same species.

120. A set of at least two kinds of polymerases for use in producing an organism having a regulated hereditary trait, wherein the polymerases have a different error-prone frequency.

121. A set according to claim 120, wherein one of the at least two kinds of polymerases is involved in an error-prone frequency of a lagging strand, and another of the at least two kinds of polymerases is involved in an error-prone frequency of a leading strand.

122. A set according to claim 121, wherein the set of polymerases are derived from the same organism species.

123. Use of at least two kinds of polymerases for regulating a conversion rate of a hereditary trait of an organism, wherein

the polymerases have a different error-prone frequency.

124. Use of at least two kinds of polymerases for producing an organism having a regulated hereditary trait, wherein the polymerases have a different error-prone frequency.